EXHIBIT E

Minimal residual disease (MRD) detection in colorectal cancer (CRC) using a plasma-only integrated genomic and epigenomic circulating tumor DNA (ctDNA) assay

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COI Disclosures for A. Parikh
SAB/Consulting: Natera, Eli Lilly, Checkmate; DSMC: Genentech/Roche ; Research to Institution: Plexxicon, Takeda, Macrogenics, Novartis, BMS, Array, Guardant, Eli Lilly

Background

- Detection of persistent circulating tumor DNA (ctDNA) after curative-intent surgery in colorectal cancer (CRC) has been shown to identify patients in minimal residual disease (MRD) who will ultimately recur. [1,2]
- Most ctDNA MRD assays require tumor sequencing to identify tumor-derived mutations to facilitate ctDNA detection, thus requiring both tumor and plasma specimens.
- This study evaluated whether the plasma-only ctDNA assay (LUNAR1, Guardant Health) can identify CRC patients with MRD post-definitive treatment.

Methods

- Prospective serial plasma specimens were obtained from 84 CRC patients undergoing curative intent surgery. 70 patients had evaluable plasma draws at landmark draw. (**Figure 2**)
- Landmark draw defined as one-month post-completion of definitive therapy (median 31.5 days); definitive therapy defined as surgery or completion of adjuvant therapy for pts who received adjuvant therapy.
- Plasma samples (2-4 mL) were evaluated using LUNAR1 (Guardant Health). LUNAR1 is a single-sample plasma-only ctDNA assay that integrated genomic and epigenomic cancer signatures with a variant classifier to differentiate tumor-derived from non-tumor derived signatures. (**Figure 1**)
- We investigated the detection of ctDNA post-definitive therapy and its relationship to clinical recurrence and recurrence-free survival.
- Additional analyses incorporated longitudinal samples available from 11 patients.

Figure 1. LUNAR1 Process

Results

Figure 2. Consort Diagram

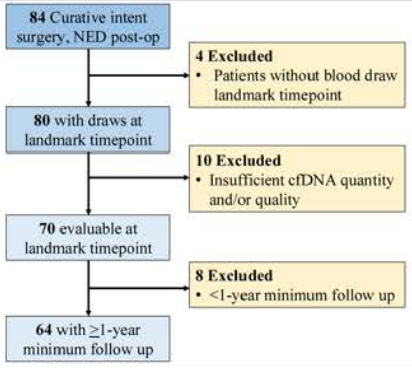

Table 1. Patient demographics and clinical characteristics

Characteristic	Overall Cohort N = 84	%
Age (years)– median (range)	60 (35-84)	
Sex		
Female	33	39.3
Male	51	60.7
Stage at Surgery		
I	8	9.5
II	20	23.8
III	40	47.6
IV	16	19.0
Sidedness		
Right	18	21.4
Transverse	5	6.0
Left	31	36.9
Rectal	30	35.7
Neoadjuvant Treatment	38	45.2
Adjuvant Treatment	46	54.8
Type of Adjuvant Treatment		
FOLFOX	30	66.7
CAPOX	7	15.6
FOLFOX + chemoxRT	3	6.7
5FU/LV	3	6.7
Other	2	4.4
Days on Adjuvant Treatment – median (range)	136 (28-463)	
Recurrences	30	35.7
Days from Surgery to Recurrence - median (range)	348.5 (35-887)	
Days of Clinical Follow Up from Surgery – median (range)	632.5 (33-1246)	

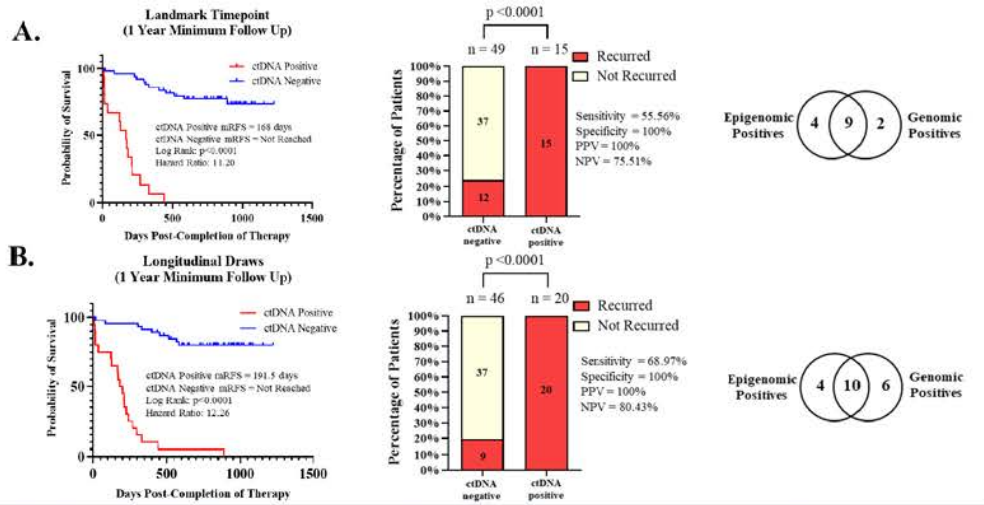

Figure 3. Recurrence-free survival, sensitivity and specificity for detection of recurrence and ctDNA positive calls (epigenomic and/or genomic) based upon ctDNA detection at landmark timepoint with 1 year-minimum follow up (a) and incorporating longitudinal draws with 1 year minimum-follow up (b).

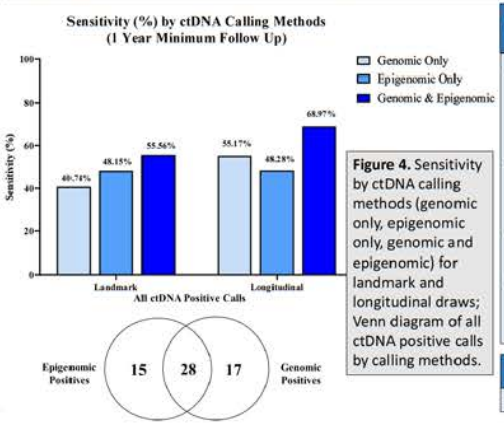

Figure 4. Sensitivity by ctDNA calling methods (genomic only, epigenomic only, genomic and epigenomic) for landmark and longitudinal draws; Venn diagram of all ctDNA positive calls by calling methods.

Conclusion

- From a single plasma sample obtained one-month post-completion of curative intent therapy in CRC patients, plasma-only ctDNA detection demonstrated favorable PPV and NPV for recurrence.
- Integrating analysis of epigenomic and genomic alterations enhanced sensitivity for MRD detection by a relative 25-36% vs. genomic alterations alone.
- Incorporating available longitudinal samples from 11 patients improved sensitivity to 69%
- These findings support the potential utility of plasma-only ctDNA detection of MRD in CRC

References

[1]Tie, *et al.* STM. 2016; [2]Reinert, *et al.* JAMA Oncol. 2019